

fee), or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

The amendments presented below are in compliance with the revised amendment format permitted in the Notice from the Office of Patent Legal Administration of the U.S. Patent and Trademark Office dated February 10, 2003, and published at 1267 OG 106 on February 25, 2003. Thus, the provisions of 37 CFR 1.121(a), (b), (c) and (d) are waived for any amendments made in this application to the claims, specification, and drawings.

**Amendments to the Claims** begin below, on this page of this document.

**Remarks/Arguments** begin on page 5 of this document.

Please amend the application as follows:

**Amendments to the Claims:**

1. (Currently Amended) A method for delivery of a therapeutic neurotrophin to damaged, diseased or defective neurons in the mammalian brain, the method comprising directly delivering a neurotrophic composition, comprising a neurotrophin encoding expression vector, into one or more delivery sites within the brain; wherein the neurotrophin is expressed in[, or within proximity to], a [targeted] cell that is, or is in proximity to, a defective, diseased or damaged neuron; and wherein further contact with the neurotrophin ameliorates the defect, disease or damage.
2. (Previously Presented) The method according to Claim 1, wherein the region of the brain containing the targeted neurons is the substantia nigra.

3. (Previously Presented) The method according to Claim 2, wherein the targeted neurons are dopaminergic neurons.
4. (Previously Presented) The method according to Claim 1, wherein the expression vector is a lentiviral vector.
5. (Previously Presented) The method according to Claim 4, wherein the neurotrophic composition is a fluid having a concentration of neurotrophin encoding viral particles in the range from  $10^{10}$  to  $10^{15}$  particles per ml of neurotrophic composition.
6. (Previously Presented) The method according to Claim 5, wherein from 2.5  $\mu$ l to 25  $\mu$ l of the neurotrophic composition is delivered to each delivery site.
7. (Previously Presented) The method according to Claim 1, wherein the treated mammal is a human and the expression vector encodes a human neurotrophin.
8. (Previously Presented) The method according to Claim 7, wherein the neurotrophin is human glial cell-derived neurotrophic factor (GDNF).
9. (Previously Presented) The method according to Claim 7, wherein the human is suffering from Parkinson's disease, and the disease is ameliorated by stimulation of growth of dopaminergic neurons.
10. (Previously Presented) The method according to Claim 9, wherein the disease is ameliorated by reversal of deficits in motor function associated with the Parkinson's disease.

11. (Previously Presented) The method according to Claim 7, wherein the human is suffering from Alzheimer's disease, and the disease is ameliorated by stimulation of growth of cholinergic neurons.
12. (Previously Presented) The method according to Claim 11, wherein the disease is ameliorated by improvement of cognitive function whose impairment was associated with Alzheimer's disease.
13. (Previously Presented) The method according to Claim 1, wherein the neurotrophin is neurturin.
14. (Previously Presented) The method according to Claim 1, wherein the neurotrophin is NGF.
15. (Previously Presented) The method according to Claim 1, wherein the neurotrophin is NT-4/5.
16. (Previously Presented) The method according to Claim 1, wherein the neurotrophin is persephin.
17. (Previously Presented) The method according to Claim 1, wherein the expression vector is an adeno-associated vector.
18. (Previously Presented) The method according to Claim 4, wherein the lentiviral expression vector is HIV-1.
19. (Previously Presented) The method according to Claim 1, wherein the neurotrophin is expressed within 500  $\mu\text{m}$  of a targeted cell.
20. (Previously Presented) The method according to Claim 1, wherein each direct delivery site is no more than 10 mm from another direct delivery site.